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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/615,116

07/07/2003

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CYTOP111

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EXAMINER

NEGIN, RUSSELL SCOTT

ART UNIT

PAPER NUMBER

1631

MAIL DATE

DELIVERY MODE

01/26/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)	
	10/615,116	COLEMAN ET AL.	
	Examiner	Art Unit	
	Russell S. Negin	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 04 January 2007.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 21, 26, 34, 39-42 and 51-75 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 21, 26, 34, 39-42 and 51-75 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## **DETAILED ACTION**

### ***Comments***

The finality in prosecution of this application is withdrawn. Prosecution is reopened. The after final amendment of 4 January 2007 is entered.

### ***Claim Rejections - 35 USC § 101***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 26, 34, 39-42, 51-60, and 63-75 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

In regards to claims 26, 34, 39-42, 51-60, and 63-75, the instant claims are drawn to a method, device, or program for an image computation. A method, device, or program for an image computation is non-statutory unless the claims include a step of physical transformation, or if the claims include a useful, tangible and concrete result. It is important to note, that the claims themselves must include a physical transformation step or a useful, tangible and concrete result in order for the claimed invention to be statutory. It is not sufficient that a physical transformation step or a useful, tangible, and concrete result be asserted in the specification for the claims to be statutory. In the instant claims, there is no step of physical transformation, thus the Examiner must determine if the instant claims include a useful, tangible, and concrete result.

In determining if the claimed subject matter produces a useful, concrete, and tangible result, the Examiner must determine each standard individually. For a claim to be "useful," the claim must produce a result that is specific, and substantial. For a claim to be "concrete," the process must have a result that is reproducible. For a claim to be "tangible," the process must produce a real world result. Furthermore, the claim must be limited only to statutory embodiments.

Claims 26, 34, 39-42, 51-60, and 63-75 do not produce a tangible result. A tangible result requires that the claim must set forth a practical application to produce a real-world result. This rejection could be overcome by amendment of the claims to recite that a result of the method is outputted to a display or a memory or another computer on a network, or by including a physical transformation.

As stated in section 2106 of the MPEP, "The tangible requirement does not necessarily mean that a claim must either be tied to a particular machine or apparatus or must operate to change articles or materials to a different state or thing. However, the tangible requirement does require that the claim must recite more than a Sec. 101 judicial exception, in that the process claim must set forth a practical application of that Sec. 101 judicial exception to produce a real-world result. *Benson*, 409 U.S. at 71-72, 175 USPQ at 676-77 (invention ineligible because had "no substantial practical application."): "[A]n application of a law of nature or mathematical formula to a . . . process may well be deserving of patent protection." *Diehr*, 450 U.S. at 187, 209 USPQ at 8 (emphasis added); see also *Corning*, 56 U.S. (15 How.) at 268, 14 L.Ed. 683 ("It is for the discovery or invention of some practical method or means of producing a

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beneficial result or effect, that a patent is granted . . ."). In other words, the opposite meaning of "tangible" is "abstract.""

***Claim Rejections - 35 USC § 103***

The rejections of claims 1-20, 22-23, 28-33, 35-38, 42-50, and 55 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus [US Patent 4,741,043] are withdrawn due to amendments filed by applicants to the set of claims filed on 4 January 2007.

The rejections of claims 23-25 and 27 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 in further view of Rumbaugh [USPAT 4,821,210] are withdrawn due to amendments filed by applicant to the set of claims filed on 4 January 2007.

The rejections of claims 23 and 24 under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus as applied to claims 1-20, 22-23, 28-33, 35-38, 43-50, and 55 in further view of Miyano et al. [USPGPUB 2003/0108230] are withdrawn due to amendments filed by applicant to the set of claims filed of 4 January 2007.

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 21, 42, 54, and 61-62 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gerlyng et al. [Cytometry, volume 13, 1992, pages 404-415] in view of Bacus [US Patent 4,741,043].

Claim 21 claims an automated method for "automatically" identifying binuclear cells and the analysis of cytokinesis to evaluate treatment.

Claim 61 limits claim 21 to a plurality of cellular features that includes nuclear features.

Claim 62 limits claim 21 to a plurality of cellular features that includes cytoplasmic features.

Claim 42 claims an automated method for "automatically" identifying binuclear cells where the binuclear cells are mutual nearest neighbors.

Claim 54 claims an automated method for "automatically" identifying binuclear cells where the binuclear cells are identified as candidate nearest neighbors.

In Gerlyng et al. Figure 1A and Table 1, the authors describe a method for identifying bi-nuclear cells by capturing an image of a plurality of marked cells. As stated on page 406, column 1, lines 22-30 and lines 34-38:

The cell monolayers were subsequently analyzed by transferring the microscope image from a Zeiss axioplan microscope equipped with a x 40 objective and a 546 nm green filter to a SEP-IPS image processing unit (Kontron, Munich, Germany) using a Grundig FA 76 video camera. The nuclear boundaries were defined by the operator by establishing a threshold grey level for each image, and pixels darker than this threshold value were identified as belonging to a nucleus.... Visual identification in the grey level image and also in the microscope directly allowed the precise identification of cell types and also classification of nuclei as belonging to mononuclear or binuclear hepatocytes.

Table 1 represents a processing and analysis of Figure 1A.

The features identified in Figure 1A of Gerlyng et al. are nuclear features with given morphologies from which nuclei can be identified. Figure 1 of Gerlyng et al. allows the identification of nuclei not only from the staining, but also the presence of concave regions around each black nucleus. In bi-nuclear cells, where two nuclei are clustered, the bi-nucleus is represented by more than one concave region in which the spatial distribution of the nuclei represents whether a binucleus exists. The proximity of the two stained regions and the number of concave regions around the nuclei (i.e. nearest neighbour first features) indicates the presence of a binucleus. In addition, next nearest neighbor regions in Figure 1A of Gerlyng et al. were identified visually to determine the presence of multinuclear features.

The non-stained regions of Figure 1A of Gerlyng et al. indicate the presence of a cytoplasmic region. The absence of a cytoplasmic region between two stained nuclei indicates the presence of a binucleus. In other words, Figure 1A of Gerlyng et al. is used as a measure of the cytoplasmic components of the cells from which the presence of binuclear cells can be identified. The intensities of the cytoplasmic versus nuclear

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component are binary in that the nuclei are gray while the cytoplasm is white. In Figure 1B of Gerlyng et al., it is the opposite: cytoplasm is black while nuclei are white; the different types of stainings used in each Figure represent a different threshold for identifying bi-nuclear cells. Figure 1A represents normal hepatocytes while Figure 1B represents regenerated hepatocytes. The binucleation index for the regenerating liver is less than 4%.

The difference between the numbers of nuclei in each picture is the effect of differences in cytokinesis (the division of cytoplasm that occurs with the division of cells) between each cell type at a given time (see Table 1 on page 407 of Gerlyng et al. for proliferation data). The images include both the nuclear and the cytoplasmic features of the cells. Since the disclosure is absent a definition of "mutual nearest neighbors," any pair of nuclei in Figure 1 of Gerlyng et al. is considered "mutual nearest neighbors." Since the disclosure is absent a definition of "candidate pairs," any pair of nuclei in Figure 1 of Gerlyng et al. is considered "candidate pairs of nuclear components."

Figures 1A and 1B of Gerlyng et al. expose a population of cells to a plurality of treatments, capture images of the plurality of cells, obtain a plurality of features from the image, analyze the plurality of cellular features (which include nuclear and cytoplasmic features) to determine the presence of bi-nuclear features. Figures 1A and 1B show determination of bi-nuclear cells from two types of image analyses.

Table 1 of Gerlyng et al. shows the classification of treatments for normal liver versus regenerating liver cells as stated in the title, "Proliferation and binucleation of hepatocytes from regenerating and normal rat liver." Table 1 also applies a statistical



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test termed a "Binucleation index" indicating abundance of bi-nuclear cells in treated versus a controlled population.

However, Gerlyng does not teach the automation aspect of the image analysis.

The patent of Bacus, entitled "Method and an apparatus for image analysis of biological specimens," states in its abstract:

A user interactive system for dynamically testing and evaluating various cells, antigens, or other materials taken from the human body. More specifically, the DNA in specimen cells is analyzed and quantified by image analysis using pattern recognition techniques. The user is provided with a unique slide or support on which there are simultaneously stained or otherwise image enhanced at the time of analysis.

Figure 1 of Bacus illustrates such a computer system which uses automation to analyze the morphology of cells. As stated in column 11, lines 34-37 (claim 24 of Bacus), "A microscopic slide for an automated cell analysis system having stored known mass characteristics for cell objects and for use in analysis of specimen cell objects,..." Such an apparatus is "[an] improved method and apparatus for analyzing cells or other biological materials by using image analysis techniques." [column 2, lines 66-68 of Bacus]

It would have been obvious to at the time of the instant invention to modify the manual binuclear imaging system of Gerlyng et al. by use of the automated cell analysis system of Bacus because while both techniques are utilized for image analysis of biological material, Bacus adds the advantage of automation and results in an improved set of image analysis techniques for biological images. It would have been further obvious to classify the treatment applied in Gerlyng et al. to liver cells in terms of its affect on cytokinesis as cytokinesis and cell reproduction are parameters used for the study and evaluation of liver regeneration in the liver cell images in Gerlyng et al.

### ***Double Patenting***

The provisional rejections of claims 1-60 under 35 U.S.C. 101 as claiming the same invention as that of claims 1-60 of copending Application No. 10/563,613 are withdrawn due to the abandonment of Application No. 10/563,613. This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. The claims between the instant and applied application are identical in their entirety.

The rejections of claims 1-60 under 35 U.S.C. 102(f) because the applicant did not invent the claimed subject matter is withdrawn due to arguments made by the applicant in page 14 of the Remarks of 4 January 2007.

### ***Conclusion***

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the central PTO Fax Center. The faxing of such pages must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993)(See 37 CFR § 1.6(d)). The Central PTO Fax Center Number is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Russell Negin, Ph.D., whose telephone number is (571) 272-1083. The examiner can normally be reached on Monday-Friday from 7am to 4pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's Supervisor, Andrew Wang, Supervisory Patent Examiner, can be reached at (571) 272-0811.

Information regarding the status of the application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

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Status information for unpublished applications is available through Private PAIR only.  
For more information on the PAIR system, contact the Electronic Business Center  
(EBC) at 866-217-9197 (toll-free).

RSN

25 January 2007

*RS*

*25 January 2007*

*John S. Brusca 25 January 2007*  
**JOHN S. BRUSCA, PH.D**  
**PRIMARY EXAMINER**